

Applicant: Soon-Shiong and Desai
Application No.: 09/628,387
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Remarks

Description of the Invention

The present invention provides a quantity of taxane in a vial which corresponds to the dosage for administration, i.e. a unit dosage form of taxane. The unit dosage forms of the present invention allow systemic administration of taxane to a human subject in need thereof at doses and over administration periods and/or treatment cycles not previously possible.

The present invention allows minimal handling of taxane by health care providers, virtually eliminates the need for costly storage and/or disposal of excess product, and reduces contamination issues for the patient. Minimal handling of taxane is recommended because, as stated in the *Drug Facts and Comparisons* (1994) at page 2785, paclitaxel, for example, is a cytotoxic anticancer drug which could be harmful to those handling the product. For example, gloves are recommended when handling paclitaxel and thorough flushing of the skin or mucous membranes with water is recommended if paclitaxel contacts the skin or mucous membranes. Minimizing the handling of taxane is therefore advantageous and is facilitated by the unit dosage forms of the present invention. For example, the need to obtain drug from multiple separate vials to create the ultimate dosage required by a subject is virtually eliminated because a single unit dosage is provided by the unit dosage form of the present invention. Similarly, the need to dispose of excess product is also eliminated. Disposal of excess product is costly both because taxane itself is very expensive and the actual disposal of excess taxane is by itself costly. Accordingly, the present invention eliminates waste of taxane by providing taxane in a unit dosage form.

Claim amendments

By the present communication, claims 1-3, 16, 58-60, 128, and 145 have been amended to define Applicants' invention with greater particularity. No new matter is introduced by the amended claim language which is fully supported by the specification and original claims. In addition, claims 4-11, 30-44, 61-73, 98-101, 104-107, 110-113, 116-119, 122-125, 133-141, 149-

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151, 153-158, 160-162, and 164-177 have been cancelled without prejudice. The amendments submitted herewith are respectfully submitted to place this application in condition for allowance, or, at a minimum, in better condition for appeal. Moreover, the claim amendments presented herein substantially reduce the total number of claims for consideration. Accordingly, entry of the claim amendments presented herein is respectfully requested.

Upon entry of the amendments submitted herewith, claims 1-3, 12-16, 58-60, 74-78, 128-131 and 145-147 will be pending.

Clarification is respectfully requested that the claims referred to in the preceding paragraph are indeed the pending claims (compare the recitation of pending claims set forth at points (4) and (6) of the "Office Action Summary" where reference is made, *inter alia* to claims up to 188).

Double Patenting Rejection

The rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-177 under the judicially created doctrine of double patenting over claims 1-57 of U.S. Patent 6,096,331 is acknowledged. The provisional rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-166, 168 and 170 under the judicially created doctrine of double patenting over claims 1-78 of co-pending Application No. 09/628,389 is also acknowledged. These rejections are obviated by the terminal disclaimer provided herewith.

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Claim Rejections Under 35 U.S.C. §112

The rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-177 under 35 U.S.C. § 112, first paragraph is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that none of the essential, defining elements which are allegedly critical or essential to the practice of the invention, are found in the claims. See Office Action at pages 3-4. While this rejection is traversed, it is respectfully submitted that this rejection is not applicable to the claims, as amended. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Claim Rejections Under 35 U.S.C. §102(b)

The rejection of claims 1-14, 16, 30-42, 44, 58-76, 78, 98, 99, 101, 104, 105, 107, 110, 111, 113, 116, 117, 119, 122, 123, 125, 128, 129, 131, 133, 135, 137-139, 141, 145, 147, 149, 151, 153-154, 156, 158, 160, 162, 164-168, 170, and 172-177 under 35 U.S.C. 102(b) as allegedly being unpatentable over pages 2780-2785 of the 1994 edition of *Drug Facts and Comparisons*, is respectfully traversed. Applicants' invention as defined, for example, by claim 1, distinguishes over this reference by requiring a unit dosage form comprising a sealed vial containing a sufficient quantity of cremophor-free taxane to provide for administration to a human subject a total dose of taxane in the range of about 30 mg/m² to about 1000 mg/m² over an administration period no greater than about 3 hours, wherein the cycle time between administrations of said total dose is less than about three weeks.

Those skilled in the art readily recognize that unit dosage forms comprising cremophor-free taxane in the range contemplated by the present claims were not available as of December 1992. Thus, the dosages mentioned in *Drug Facts and Comparisons* (i.e., 135 mg/m² to 175 mg/m²) were not provided without cremophor, in a single vial (i.e., unit dosage form), as required by the present claims. Clearly, only the present invention teaches unit dosage forms comprising cremophor-free taxane in the range of about 30 mg/m² to about 1000 mg/m² for

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administration over three hours, wherein the cycle time between administrations of said total dose is less than about three weeks.

Applicants respectfully disagree with the Examiner's assertion that *Drug Facts and Comparisons* discloses paclitaxel in single dose vials and that this disclosure anticipates the claims of the present invention. See Office Action, page 6. Contrary to the Examiner's assertion, the single dose vial referred to in the reference is not the same as a unit dosage form; it is only used to store diluted paclitaxel solutions that have been prepared in non-plasticized containers, in order to prevent DEHP (di-ethylhexylphthalate) leaching. Clearly, the prior art does not teach a unit dosage form, instead requiring that one "*Premedicate all patients prior to administration in order to prevent severe hypersensitivity reactions*" (p. 2785). The prior art indicates that such reactions are due to the presence of cremophor in the formulation (see pp. 2781 and 2785-footnote). The prior art further recommends that plasticized PVC equipment not be used, in order to minimize patient exposure to DEHP, which can be leached from PVC infusion bags or sets. In addition, the art recommends the storage of diluted paclitaxel in glass bottles and administration through polyethylene-lined administration sets (see p. 2785).

Accordingly, the prior art does not anticipate Applicants' invention, as claimed, because the art does not teach the use of a cremophor-free, unit dosage form of paclitaxel, which may be administered via standard i.v. tubing, without pre-medication of patients, using plasticized containers.

The rejection of claims 1-15, 30-43, 58-77, 98-100, 104-106, 110-112, 116-118, 122-124, 128-130, 133-134, 137-140, 145-146, 149-150, 153-157, 160-161, 164-171 and 177 as allegedly being anticipated by page 3558 of *Drug Facts and Comparisons* is respectfully traversed. The fact that this reference recommends particular dosages of docetaxel is irrelevant. What is embraced, for example, by claim 1 is a unit dosage form comprising a sealed vial with a specified quantity of cremophor-free taxane. The reference does not disclose a unit dosage form of a cremophor-free taxane. Because *Drug Facts and Comparisons* does not teach the unit

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dosage forms of the present invention and does not teach the administration protocol contemplated for use with invention unit dosage forms, the rejection of claims 1-15, 30-43, 58-77, 98-100, 104-106, 110-112, 116-118, 122-124, 128-130, 133-134, 137-140, 145-146, 149-150, 153-157, 160-161, 164-171 and 177 under 35 U.S.C. 102(b) is not properly applied. Accordingly, reconsideration and withdrawal are respectfully requested.

Claim Rejections Under 35 U.S.C. §103

The rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-177 under 35 U.S.C. § 103 as allegedly being unpatentable over pages 2780-2785 or page 3558 of *Drug Facts and Comparisons* is respectfully traversed. Applicants' invention, as defined for example by claim 1, distinguishes over *Drug Facts and Comparisons* by requiring a unit dosage form comprising a sealed vial containing a sufficient quantity of cremophor-free taxane to provide for administration to a subject a total dose of cremophor-free taxane in the range of about 30 mg/m² to about 1000 mg/m² over an administration period no greater than about 3 hours. In contrast, *Drug Facts and Comparisons* does not teach or suggest unit dosage forms comprising cremophor-free taxane.

In addition, Applicants respectfully submit that the disclosure on either pages 2780-2785 or page 3558 of *Drug Facts and Comparisons* does not fairly suggest the unit dosage forms required by, for example, claim 1. Those skilled in the art would not be motivated to produce a unit dosage form as required by claim 1. One of skill in the art did not have any motivation as of the filing date to prepare a unit dosage form containing a total dose of cremophor-free taxane in the specified range of 30 mg/m² to about 1000 mg/m² over an administration period of no greater than 3 hours. Thus, it is respectfully submitted that the rejection under 35 U.S.C. 103(a) is not properly applied. Accordingly, reconsideration and withdrawal of the rejection of claims 1-16, 30-44, 58-78, 98-101, 104-107, 110-113, 116-119, 122-125, 128-131, 133-135, 137-141, 145-147, 149-151, 153-158, 160-162, 164-177 are respectfully requested.

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In view of the above remarks, reconsideration and favorable action on all claims are respectfully requested. If any matters remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the telephone number set forth below so that a prompt disposition of this application can be achieved.

Respectfully submitted,



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